I. AMENDMENTS

The following Listing of the Claims replaces all prior versions, listings and amendments.

Claims 1. to 16. (Canceled).

17. (Previously Presented) The method of claim 26, further comprising contacting the cell with an effective amount of a compound that diminishes intracellular thymidine or purine, wherein said compound is 6-mercaptopurine, thioguanine, or 2'-deoxycoformycin.

18. (Canceled).

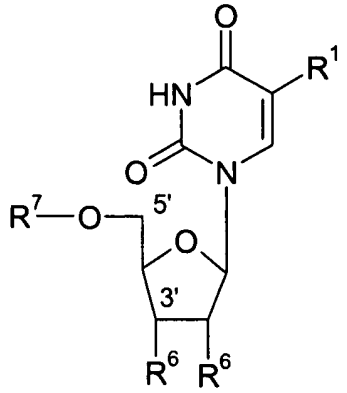
19. (Currently Amended) The method of 26, wherein the compound is (E)-5-(2-bromovinyl)-2'-deoxy-5'-uridyl phenyl L-alaninylphosphoramidate or (E)-5-(2-bromovinyl)-2'-deoxy-5'-uridyl phenyl ~~L-alaninyl~~ monophosphate.

20. (Currently Amended) A method for screening for therapeutic agents for ~~use~~ administration in combination with (E)-5-(2-bromovinyl)-2'-deoxy-5'-uridyl phenyl L-alaninylphosphoramidate or (E)-5-(2-bromovinyl)-2'-deoxy-5'-uridyl phenyl L-alaninyl monophosphate, comprising contacting the candidate therapeutic agent and (E)-5-(2-bromovinyl)-2'-deoxy-5'-uridyl phenyl L-alaninylphosphoramidate or (E)-5-(2-bromovinyl)-2'-deoxy-5'-uridyl phenyl ~~L-alaninyl~~ monophosphate with a hyperproliferative cell that overexpresses endogenous, intracellular thymidylate synthase enzyme and assaying for cell death.

21. (Currently Amended) The method of claim 20, further comprising contacting a normal cell with the candidate therapeutic agent and (E)-5-(2-bromovinyl)-2'-deoxy-5'-uridyl phenyl L-alaninylphosphoramidate or (E)-5-(2-bromovinyl)-2'-deoxy-5'-uridyl phenyl ~~L-alaninyl~~ monophosphate and assaying for cell death.

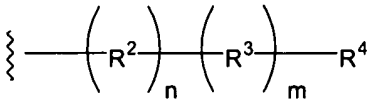
Claims 22. to 25. (Canceled).

26. (Currently Amended) A method for inhibiting the proliferation of a cancer cell that endogenously overexpresses thymidylate synthase and wherein the cancer cell is selected from the group consisting of skin, bone, bone marrow, testis, brain, liver, lung, prostate and ovary, the method comprising contacting the cell with an effective amount of a compound having the structure:



wherein:

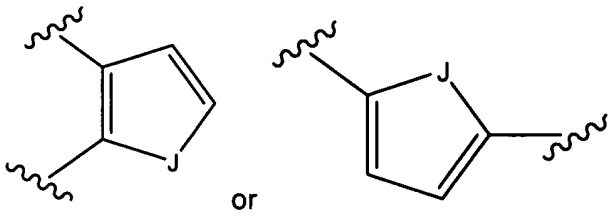
R^1 is of the formula:



wherein R^2 is one of:

an unsaturated C2 to C4 hydrocarbyl group;

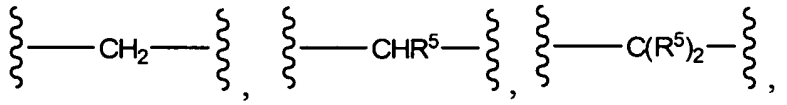
a heteroaromatic group having the structure:

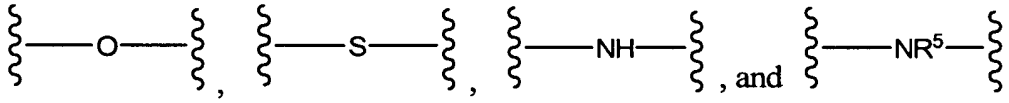


or

wherein J is -O-, -S-, -Se-, -NH-, or -NRALK-, wherein RALK is a linear or branched alkyl having 1 to 10 carbon atoms or a cycloalkyl group having 3 to 10 carbon atoms;

R^3 is selected from the group consisting of:



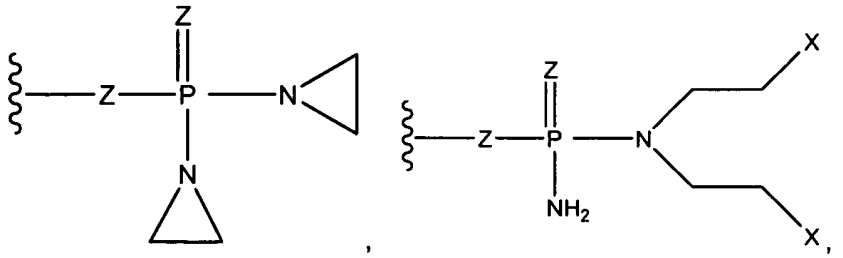


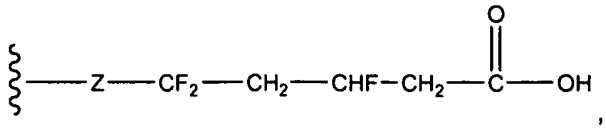
wherein R^5 may be the same or different and is independently a linear or branched alkyl group having from 1 to 10 carbon atoms, or a cycloalkyl group having from 3 to 10 carbon atoms;

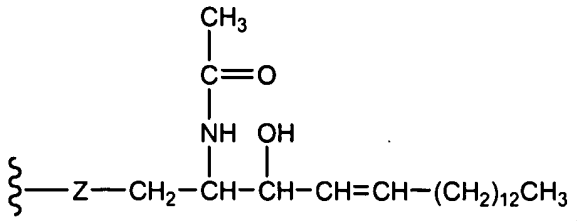
wherein n is an integer from 1 to 10;

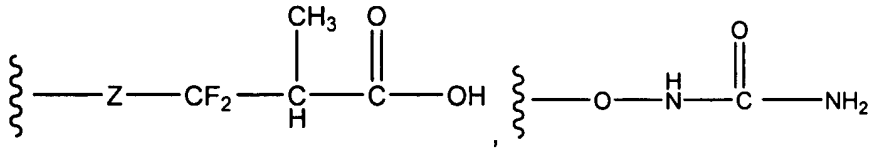
wherein m is 0 or 1;

wherein R^4 is a toxophore selected from the group consisting of:

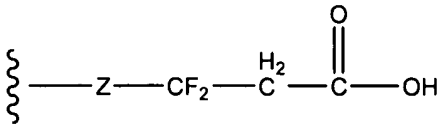








, and



wherein X is -Cl, -Br, -I, or other halogen, with the proviso that when R^7 is -H, and m is zero, then R^4 is not a halogen or when m is zero and n is zero, then R^4 is not a halogen;

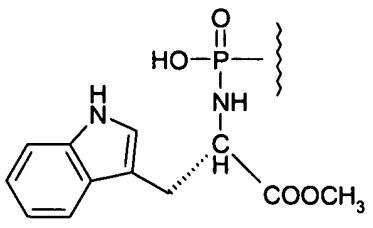
~~wherein Y is independently -H or -F;~~

wherein Z is independently -O- or -S-;

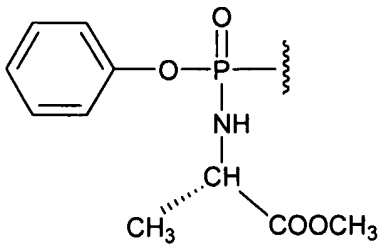
wherein R^7 is hydrogen, a monophosphate or a phosphoramidatyl derivative of an amino acid;

and wherein said compound may be in any enantiomeric, diasteriomeric, or stereoisomeric form, consisting of a D-form, L-form, α-anomeric form, and β-anomeric form.

27. (Previously Presented) The method of claim 26, wherein, R^7 is:

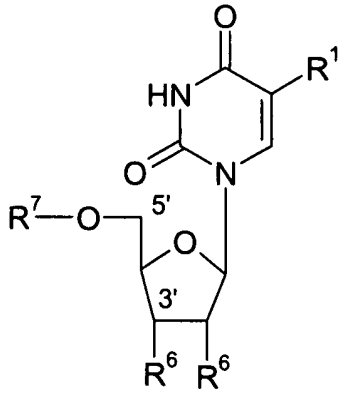


or



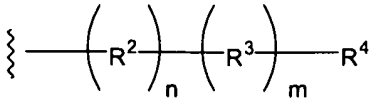
28. (Currently Amended) The method of claim 26, wherein X is -Cl, -Br, or -I.

29. (Currently Amended) A method for inhibiting the proliferation of a cancer cell that endogenously overexpresses thymidylate synthase, the method comprising contacting the cell with an effective amount of a compound that inhibits thymidylate synthase activity, subsequent to contacting the cell with an effective amount of a compound having the structure:



wherein:

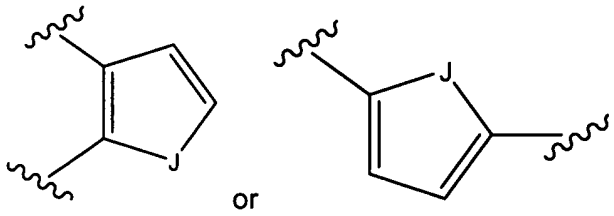
R^1 is of the formula:



wherein R^2 is one of:

an unsaturated C2 to C4 hydrocarbyl group;

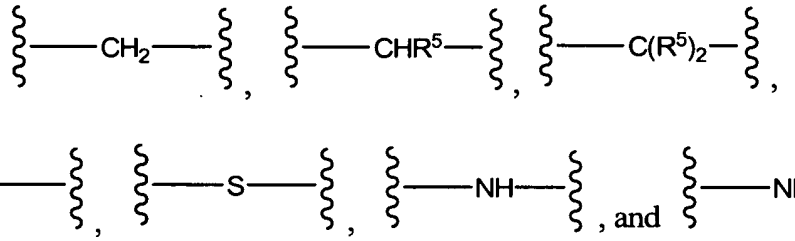
a heteroaromatic group having the structure:



or

wherein J is -O-, -S-, -Se-, -NH-, or -NRALK-, wherein RALK is a linear or branched alkyl having 1 to 10 carbon atoms or a cycloalkyl group having 3 to 10 carbon atoms;

R^3 is selected from the group consisting of:

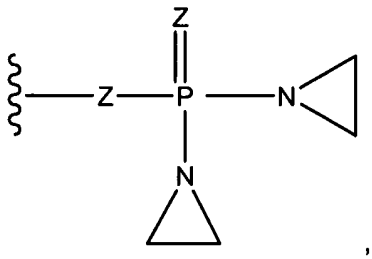


wherein R^5 may be the same or different and is independently a linear or branched alkyl group having from 1 to 10 carbon atoms, or a cycloalkyl group having from 3 to 10 carbon atoms;

wherein n is an integer from 1 to 10;

wherein m is 0 or 1;

wherein R^4 is a toxophore selected from the group consisting of:



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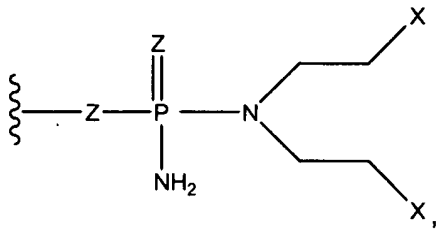

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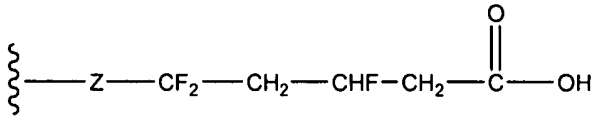

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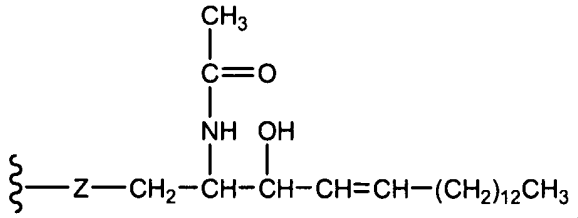

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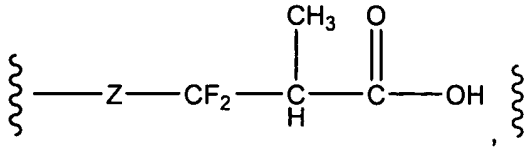

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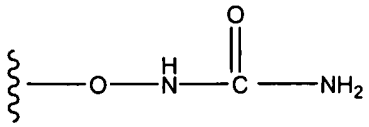

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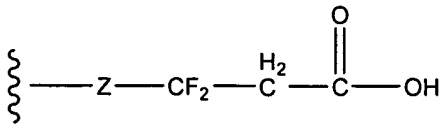


,

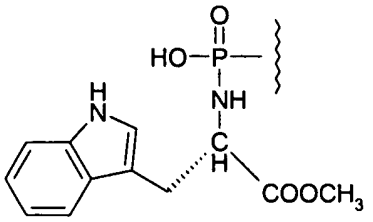
wherein X is -Cl, -Br, -I, or other halogen, with the proviso that when R^7 is -H, and m is zero, then R^4 is not a halogen or when m is zero and n is zero, then R^4 is not a halogen;

~~wherein Y is independently -H or -F;~~

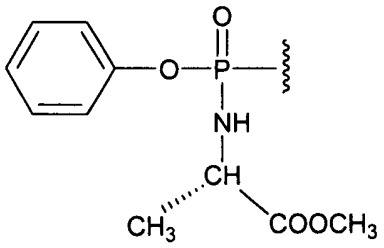
wherein Z is independently -O- or -S-; wherein R^7 is hydrogen, a monophosphate or a phosphoramidatyl derivative of an amino acid;

and wherein said compound may be in any enantiomeric, diasteriomeric, or stereoisomeric form, consisting of a D-form, L-form, α-anomeric form, and β-anomeric form.

30. (Previously Presented) The method of claim 29, wherein, R^7 is:



or



31. (Currently Amended) The method of claim 29, wherein X is -Cl, -Br, or -I.

32. (Currently Amended) The method of claim 29, wherein the compound is (E)-5-(2-bromovinyl)-2'-deoxy-5'-uridyl phenyl L-alaninylphosphoramidate or (E)-5-(2-bromovinyl)-2'-deoxy-5'-uridyl phenyl ~~L-alaninyl~~ monophosphate.

33. (Previously Presented) The method of claims 26 or 29, wherein the contacting is in vivo by administration to a subject in need thereof.

34. (Currently Amended) The method of claim 20, wherein the candidate

therapeutic agent is contacted with the cell subsequent to contacting the cell with (E)-5-(2-bromovinyl)-2'-deoxy-5'-uridyl phenyl L-alaninylphosphoramidate or (E)-5-(2-bromovinyl)-2'-deoxy-5'-uridyl phenyl ~~L-alaninyl~~ monophosphate.

35. (Currently Amended) The method of claim 20, wherein the cell is resistant to (E)-5-(2-bromovinyl)-2'-deoxy-5'-uridyl phenyl L-alaninylphosphoramidate or (E)-5-(2-bromovinyl)-2'-deoxy-5'-uridyl phenyl ~~L-alaninyl~~ monophosphate.

36. (New) The method of claim 29, wherein the compound that inhibits thymidylate synthase activity is 5-Fluorouracil or Tomudex.